

## TELEFACSIMILE LETTER FROM

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Application of: Brines *et al.*

Confirmation No.: 7619

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Art Unit: 1647

Filed: January 3, 2005

Examiner: WOODWARD, Cherie Michelle

For: TISSUE PROTECTIVE CYTOKINES FOR THE  
PROTECTION, RESTORATION, AND  
ENHANCEMENT TO RESPONSE CELLS

Attorney Dock et No: 10165-037-999  
(Formerly: KW00-2B02-US)

Dear Examiner Woodward,

To follow up on the in-person interview on February 4, 2009 in connection with the above-identified patent application, please find attached a proposed claim 8 and new claim 54 for your consideration. Please contact us to set up a time to discuss whether our proposed claim amendment reflect your suggested claim amendment.

Sincerely,  
Eileen F. Falvey  
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8. (Currently amended) A method for treating an inflammatory disease in a mammal comprising administering to a mammal in need thereof a prophylactically or therapeutically effective amount of a chemically modified erythropoietin and an anti-inflammatory agent or a prophylactically or therapeutically effective amount of a chemically modified erythropoietin and an immunomodulatory agent,

wherein said chemically modified erythropoietin has a reduced level of in vivo erythropoietic activity compared to native erythropoietin as determined by the exhypoxic polycythemic mouse bioassay, and has tissue protective activity in vivo as determined by the middle cerebral artery occlusion test,

and wherein said chemically modified erythropoietin comprises:

- i) a chemically modified arginine residue at position 31, 37, 41, 80, 103, 130, 137, 158, 166, 170, 177, 189, or 193 of SEQ ID NO:5;
- ii) a chemically modified lysine residue at position 47, 72, 79, 124, 143, 167, 179, or 181 of SEQ ID NO:5 or a chemically modified N-terminal amino group;
- iii) a chemically modified tyrosine residue at position 42, 76, 172, or 183 of SEQ ID NO:5;
- iv) a chemically modified aspartic acid residue at position 35, 70, 123, 150, 163, or 192 of SEQ ID NO:5;
- v) a chemically modified glutamic acid residue at position 40, 45, 48, 50, 58, 64, 82, 89, 99, 116, 144, or 186 of SEQ ID NO:5; and
- v) a chemically modified tryptophan residue at position 78, 91, or 115 of SEQ ID NO:5,

wherein the chemical modification results from one of the following chemical reactions: acetylation; carbamylation; succinylation; carboxymethyllysination; alkylation; nitration; iodination; biotinylation; a reaction with n-bromosuccinimide, chlorosuccinimide, vicinal diketone, or glyoxal; a reaction with R-glyoxal wherein R is selected from the group consisting of aryl, heteroaryl, lower alkyl, lower alkoxy, cycloalkyl group, and alpha-deoxyglycitoyl; or a reaction with carbodiimide followed by reaction with an amine.

54. (New) A method for treating an inflammatory disease in a mammal comprising administering to a mammal in need thereof a prophylactically or therapeutically effective amount of a chemically modified erythropoietin, wherein said chemically modified erythropoietin has a reduced level of in vivo erythropoietic activity compared to native erythropoietin as determined by the exhypoxic polycythemic mouse bioassay, and has tissue protective activity in vivo as determined by the middle cerebral artery occlusion test, and wherein said chemically modified erythropoietin comprises:

- i) a chemically modified arginine residue at position 31, 37, 41, 80, 103, 130, 137, 158, 166, 170, 177, 189, or 193 of SEQ ID NO:5;
- ii) a chemically modified lysine residue at position 47, 72, 79, 124, 143, 167, 179, or 181 of SEQ ID NO:5 or a chemically modified N-terminal amino group;
- iii) a chemically modified tyrosine residue at position 42, 76, 172, or 183 of SEQ ID NO:5;
- iv) a chemically modified aspartic acid residue at position 35, 70, 123, 150, 163, or 192 of SEQ ID NO:5;
- v) a chemically modified glutamic acid residue at position 40, 45, 48, 50, 58, 64, 82, 89, 99, 116, 144, or 186 of SEQ ID NO:5; and
- v) a chemically modified tryptophan residue at position 78, 91, or 115 of SEQ ID NO:5;

wherein the chemical modification results from one of the following chemical reactions: acetylation; carbamylation; succinylation; carboxymethyllysination; alkylation; nitration; iodination; biotinylation; a reaction with n-bromosuccinimide, chlorosuccinimide, vicinal diketone, or glyoxal; a reaction with R-glyoxal wherein R is selected from the group consisting of aryl, heteroaryl, lower alkyl, lower alkoxy, cycloalkyl group, and alpha-deoxyglycitoyl; or a reaction with carbodiimide followed by reaction with an amine.